

amino-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, hydroxy-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, lower ( $C_1-C_4$ ) alkoxy-carbonyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, lower ( $C_1-C_4$ ) alkylimino-substituted ( $C_1-C_6$ ) alkyl, lower ( $C_1-C_4$ ) acylimido-ylimino-substituted ( $C_1-C_6$ ) alkyl, arylmethylimino-substituted ( $C_1-C_6$ ) alkyl, nitrogen-containing heterocyclic radical-substituted lower ( $C_1-C_4$ ) alkylimino-substituted ( $C_1-C_6$ ) alkyl, nitrogen-containing heterocyclic radical-substituted lower ( $C_1-C_4$ ) alkyl, oxygen-containing ( $C_1-C_8$ ) straight chain or branched alkyl, arylsulfonamido-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, alkylsulfonamido-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, aryloxy-substituted lower ( $C_1-C_4$ ) alkyl, and hydroxy-substituted ( $C_1-C_8$ ) alkyl;

$R^4$  is selected from the group consisting of ( $C_3-C_9$ ) alkyl, hydroxy-substituted ( $C_3-C_8$ ) alkyl, and unsubstituted or optionally substituted aryl-lower ( $C_1-C_4$ ) alkyl;

$R^5$  is selected from the group consisting of lower ( $C_1-C_4$ ) alkyl, ( $C_3-C_7$ ) cycloalkyl, mono- or di-lower ( $C_1-C_4$ ) alkylamino-substituted lower ( $C_1-C_4$ ) alkyl, carboxy-substituted lower ( $C_1-C_4$ ) alkyl, hydroxy-substituted ( $C_1-C_6$ ) alkyl, bis(phosphono)-hydroxymethyl-substituted ( $C_1-C_{11}$ ) alkyl, tetrabenzyl bis(phosphono)hydroxymethyl-substituted ( $C_1-C_{11}$ ) alkyl, and a nitrogen-containing heterocyclic radical;

$R^6$  is hydrogen;

$R^7$  is hydrogen or lower ( $C_1-C_4$ ) alkyl;

$R^8$  is hydrogen or lower ( $C_1-C_4$ ) alkyl; and

$R^9$  is selected from the group consisting of hydrogen, hydroxy, amino, and a group of the formula:  $-X-Y$

wherein X is ( $C_1-C_6$ ) alkylene or phenylene, and

Y is a group of the formula:  $-A-B$  or  $-B$

wherein B is selected from the group consisting of hydrogen, amino, amidino, lower ( $C_1-C_4$ ) acylimido-yl, unsubstituted or

optionally substituted benzimidoyl, bis(phosphono)methyl, tetra-lower ( $C_1-C_4$ ) alkyl bis(phosphono)methyl, tri-lower ( $C_1-C_4$ ) alkyl bis(phosphono)methyl, bis(phosphono)hydroxymethyl, tetrabenzyl bis(phosphono)hydroxymethyl, and lower ( $C_1-C_4$ ) alkyl-substituted imidazol-3-yl, and

A is selected from the group consisting of lower ( $C_1-C_4$ ) alkylene, imino, and lower ( $C_1-C_4$ ) alkylene-imino;

provided that a combination wherein  $R^7$  is methyl,  $R^8$  is methyl and  $R^9$  is methyl is excluded;

or a pharmaceutically acceptable salt or solvate thereof.

3. (Amended) The compound according to claim 2, wherein

$R^1$  and  $R^2$  are hydrogen;

$R^3$  is selected from the group consisting of methyl, isobutyl, aminopropyl, phenylpropyl, guanidophenylpropyl, aminophenylpropyl, hydroxyphenylpropyl, carboxyphenylpropyl, carbamoylphenylpropyl, aminomethylphenylpropyl, guanidomethylphenylpropyl, hydroxymethylphenylpropyl, aminomethylbenzyl, toluenesulfonamidomethylbenzyl, methanesulfonamidomethylbenzyl, isobutyliminomethylbenzyl, phthalimidomethylbenzyl, phenoxyethyl, aminopentyl, acetimidoyliminopentyl, isobutyliminopentyl, pyridylmethyliminopentyl, methoxycarbonylphenylpropyl, ethoxyethoxyethyl, hydroxyoctyl, butoxyethyl, isobutyloxyethyl, morpholinopropyl, (3,4,4-trimethyl-2,5-dioxo-imidazolidin-1-yl)propyl, cyclohexylpropyl, and piperidinopropyl;

$R^4$  is selected from the group consisting of naphthylmethyl, phenylpropyl, isobutyl, tert-butyl, isopropyl, and hydroxyoctyl;

$R^5$  is selected from the group consisting of methyl, cyclopropyl, 2-(N,N-dimethylamino)ethyl, 2-carboxyethyl, 2-hydroxyethyl, 2-hydroxy-1,1-dimethylethyl, 2-hydroxy-1-methylethyl, 6,6-bis(phosphono)-6-hydroxyhexyl, tetrabenzyl 6,6-bis(phosphono)-6-hydroxyhexyl, piperidyl, and morpholinyl;

$R^6$  is hydrogen;

$R^7$  is hydrogen or methyl;

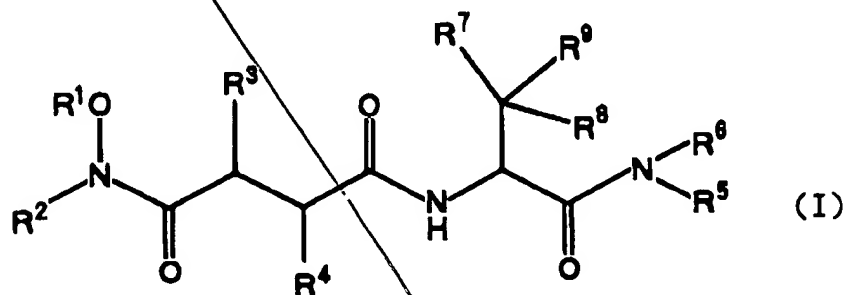
$R^8$  is hydrogen or methyl; and

$R^9$  is selected from the group consisting of hydrogen, hydroxy, amino, and a group of the formula:  $-X-Y$  wherein  $X$  is selected from the group consisting of methylene, ethylene, trimethylene, tetramethylene, pentamethylene, hexamethylene, and phenylene, and

$Y$  is a group of the formula:  $-A-B$  or  $-B$  wherein  $B$  is selected from the group consisting of amino, amidino, acetimidoyl, propionimidoyl, benzimidoyl, bis(phosphono)methyl, tetraethyl bis(phosphono)methyl, triethyl bis(phosphono)methyl, tetramethyl bis(phosphono)methyl, trimethyl bis(phosphono)methyl, bis(phosphono)hydroxymethyl, tetrabenzyl bis(phosphono)hydroxymethyl, and 2-methyl-imidazol-3-yl, and

$A$  is selected from the group consisting of imino, methyleneimino, and methylene.

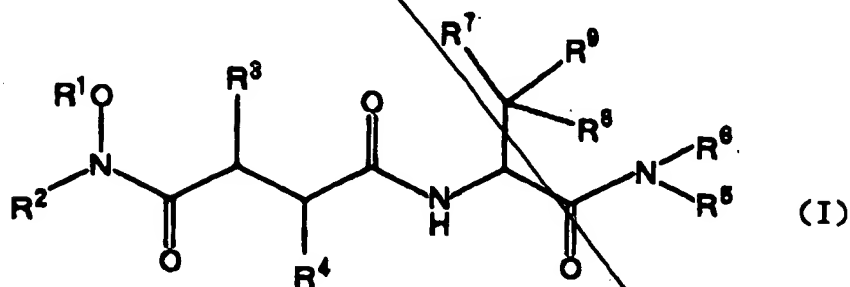
4. (Amended) A pharmaceutical or veterinary composition which comprises (a) an effective amount of at least a member selected from the group consisting of a compound of the formula (I):



wherein  $R^1$  to  $R^9$ , all have the same meanings as defined in claim 2, and a pharmaceutically or veterinarily acceptable salt or solvate thereof, and (b) a pharmaceutically or veterinarily acceptable excipient or carrier.

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B1  
COO-t.  
All  
cancel

5. (Amended) A metalloproteinase inhibitor which comprises an effective amount of at least a member selected from the group consisting of a compound of the formula (I):

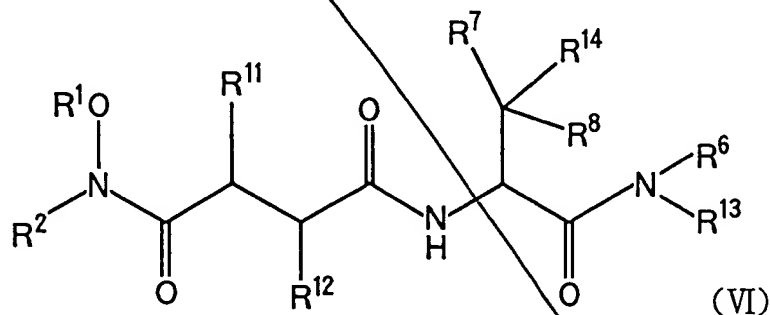


wherein  $R^1$  to  $R^9$ , all have the same meanings as defined in claim 2, and a pharmaceutically acceptable salt or solvate thereof.

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B2  
A12

8. (Amended) A method of prophylactically and/or therapeutically treating diseases and/or disorders associated with tissue degradation comprising administering an effective amount of the compound according to claim 2.

12. (Amended) A compound having the following formula (VI):



A13

SUB  
B3

wherein  $R^1$ ,  $R^2$ , and  $R^6$  to  $R^8$ , all have the same meanings as defined in claim 2,

SUB  
B3  
COD 4  
A13

$R^{11}$  has the same meaning as defined for  $R^3$ , or is selected from the group consisting of protected hydroxy, protected guanido-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected amino-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, nitro-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected amino-substituted ( $C_1-C_6$ ) alkyl, nitro-substituted ( $C_1-C_6$ ) alkyl, protected carboxy-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected hydroxy-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected guanido-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected amino-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected hydroxy-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected carboxy-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected hydroxy-containing ( $C_1-C_8$ ) straight chain or branched alkyl, and cyano-substituted phenyl-lower ( $C_1-C_4$ ) alkyl;

$R^{12}$  has the same meaning as defined for  $R^4$ , or is protected hydroxy-substituted ( $C_1-C_8$ ) alkyl;

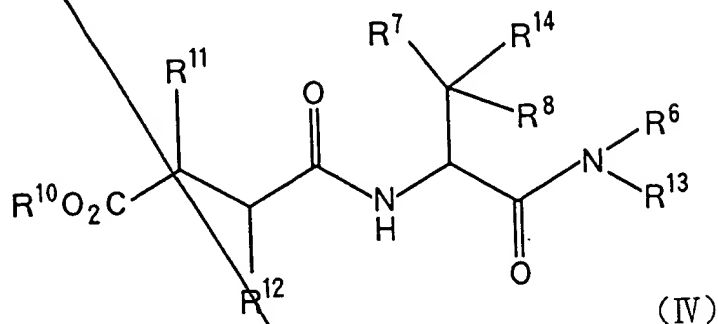
$R^{13}$  has the same meaning as defined for  $R^5$ , or is selected from the group consisting of protected carboxy-substituted lower ( $C_1-C_4$ ) alkyl, protected hydroxy-substituted lower ( $C_1-C_4$ ) alkyl, protected bis(phosphono)hydroxymethyl-substituted ( $C_1-C_{11}$ ) alkyl, and a protected nitrogen-containing heterocyclic group; and

$R^{14}$  has the same meaning as defined for  $R^9$ , or is selected from the group consisting of protected amino, protected hydroxy, and a group of the formula:  $-X-E$  or  $-X-A-E$

wherein X and A, both have the same meanings as given above, and E is selected from the group consisting of nitro, cyano, amino, carboxyl, ( $C_1-C_{11}$ ) hydroxyalkyl, protected amino, protected guanido, protected amidino, protected acylimido, protected benzimidoyl, protected bis(phosphono)methyl, protected bis(phosphono)hydroxymethyl, and protected ( $C_1-C_{11}$ ) alkyl-substituted imidazol-3-yl;

or a salt thereof.

13. (Amended) A compound having the following formula (IV):



wherein  $R^6$  to  $R^8$ , all have the same meanings as defined in claim

2,

$R^{10}$  is selected from the group consisting of unsubstituted or optionally substituted alkyl, unsubstituted or optionally substituted aralkyl, and a carboxy-protecting group;

$R^{11}$  has the same meaning as defined for  $R^3$ , or is selected from the group consisting of protected hydroxy, protected guanido-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected amino-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, nitro-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected amino-substituted ( $C_1-C_6$ ) alkyl, nitro-substituted ( $C_1-C_6$ ) alkyl, protected carboxy-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected hydroxy-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected guanido-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected amino-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected hydroxy-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected carboxy-substituted lower ( $C_1-C_4$ ) alkyl-substituted phenyl-lower ( $C_1-C_4$ ) alkyl, protected hydroxy-containing ( $C_1-C_8$ ) straight chain or branched alkyl, and cyano-substituted phenyl-lower ( $C_1-C_4$ ) alkyl;

$R^{12}$  has the same meaning as defined for  $R^4$ , or is protected hydroxy-substituted ( $C_1-C_8$ ) alkyl;

bis(phosphono)methyl, protected bis(phosphono)hydroxymethyl,  
and protected (C<sub>1</sub>-C<sub>11</sub>) alkyl-substituted imidazol-3-yl,

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B3  
CD 24  
R<sup>13</sup> has the same meaning as defined for R<sup>5</sup>, or is selected from the group consisting of protected carboxy-substituted lower (C<sub>1</sub>-C<sub>4</sub>) alkyl, protected hydroxy-substituted lower (C<sub>1</sub>-C<sub>4</sub>) alkyl, protected bis(phosphono)hydroxymethyl-substituted (C<sub>1</sub>-C<sub>11</sub>) alkyl, and a protected nitrogen-containing heterocyclic group; and

A13  
cancel  
R<sup>14</sup> has the same meaning as defined for R<sup>9</sup>, or is selected from the group consisting of protected amino, protected hydroxy, and a group of the formula: -X-E or -X-A-E

wherein X and A, both have the same meanings as given above, and E is selected from the group consisting of nitro, cyano, amino, carboxyl, (C<sub>1</sub>-C<sub>11</sub>) hydroxyalkyl, protected amino, protected guanido, protected amidino, protected acylimido, protected benzimidoyl, protected

or a salt thereof.

#### REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Claim 1 has been cancelled without prejudice, claim 2 has been amended to more particularly define the present invention, and claims 3-5, 8, 12 and 13 have been amended to depend on claim 2. Further, claims 12 and 13 have been amended to specifically recite R<sup>10</sup> to R<sup>14</sup>